

REMARKS

Claims 1-11, 19, 25, 31, and 44 were pending, and claims 1-11, 19, and 31 are currently under examination. By this amendment claims 1, 11, 19, and 31 are amended; no claims are canceled; and no new claims are added. No new matter is introduced.

Each of claims 1, 11, 19, and 31 is currently amended to specify that the compositions used in the claimed methods are isolated HSP60, isolated HSP65, or therapeutically effective fragments or peptide analogs thereof.

Objection to IDS

The Examiner indicated that the IDS submitted 11 June 2002 was incomplete and therefore failed to comply with provisions of 37 C.F.R. 1.97, 1.98, and MPEP § 609 because, at the time the Office Communication was mailed, copies of foreign patents listed as B11 to B12 and publications listed as C1 through C36 were absent. However, following a telephone interview between Applicants' representative and the Examiner about this matter on October 20, 2003, the Examiner found all the missing references. Applicants' representative thanks Examiner Liu for his indication, communicated in a voicemail on November 12, 2003, that he had located and will consider all art cited in the Form 1449 included with the IDS submitted 11 June 2002.

Specification Objections

The specification has been amended as required by the Examiner to spell out in each of their first instance of use, the terms HSP65, BSA, and OCT. The term PBS is spelled out at its first instance of use on page 25, lines 21-22. The term ELISA is spelled out at its first instance of use on page 22, lines 27-28. The term CFA is spelled out at its first instance of use at page 6, line 7. In addition, the embedded hyperlinks on page 13 have been removed. In view of the foregoing amendments to the specification, Applicants respectfully request withdrawal of the specification objections.

• *Claim Rejections Under 35 U.S.C. § 112, second paragraph*

The Examiner indicated that claims 1-11, 19, and 31 are rejected for allegedly failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. More specifically, the Examiner asserts that recitation of “analog of a heat shock protein” is indefinite because, in the Examiner’s view, the specification does not define the “analog” and the recitation is unclear as to whether or not the said analog encompasses any non-proteinous molecule or any protein mimics of HSP.

In response, Applicants first wish to direct the Examiner’s attention to the passage at pages 22-23 which expressly sets forth a definition for “therapeutically effective analog”, as used in claims 1, 11, 19, and 31. As provided there, the term “therapeutically effective analogs” of heat shock proteins or fragments thereof refers, *inter alia*, to compounds that are structurally related to heat shock protein peptides or to their therapeutically effective fragments (e.g., inflammatory response-suppressive fragments) and which possess the same biological activity, i.e., the ability to treat the condition, e.g., by eliminating or suppressing the inflammatory response, upon mucosal administration, either nasally, orally, or enterally. By way of non-limiting example, the term is further set forth to include peptides having amino acid sequences which differ from the amino acid sequence of the heat shock protein peptide or therapeutically effective fragments thereof by one or more amino acid residues while still retaining the inflammatory response-suppressive activity of the heat shock protein peptide or fragment. Therefore, Applicants respectfully submit that the term “analog” as used in claims 1-11, 19, and 31 is not indefinite because the specification does define the “analog”.

Second, without meaning to concede the Examiner’s argument, and solely for the purpose of advancing prosecution, Applicants have amended claims 1-11, 19, and 31 to further specify that the analogs are peptides. Support for this amendment is recited in the previous paragraph.

In view of the foregoing, Applicants submit that claims 1-11, 19, and 31 do not fail to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. Therefore, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph of claims 1-11, 19, and 31.

• *Claim Rejections Under 35 U.S.C. § 112, first paragraph*

The Examiner indicated that claims 1-7, 11, 19, and 31 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Applicants note, however, that the Examiner acknowledged, on page 4 of the Office Communication, that the specification is enabling for a process of treating a vascular disorder in a mammal comprising administering to a mucosal surface a composition comprising HSP60 or HSP65 or a fragment of HSP65. For reasons stated below, Applicants request withdrawal of the rejection of claims 1-7, 11, 19, and 31 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement.

As noted above, claims 1, 11, 19, and 31 are currently amended to specify that the compositions are isolated HSP60, isolated HSP65, or therapeutically effective fragments or peptide analogs thereof. Applicants submit that the present amendments address the enablement rejections because the Examiner has said as much.

Applicants therefore respectfully request withdrawal of the rejection of claims 1-7, 11, 19, and 31 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement.

Claim Rejections Under 35 U.S.C. § 103(a)

The Examiner indicated that claims 1, 3-7, 11, 19, and 31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Srivastava et al. (US Pat. No. 6,007,821) taken with Wick et al. (*Am Heart J* (1999) 138:S444-9). For reasons stated below, Applicants respectfully disagree and therefore request withdrawal of the rejection of claims 1, 3-7, 11, 19, and 31 under 35 U.S.C. § 103(a).

Applicants submit that the Examiner has failed to make a *prima facie* case for making the obviousness rejection. First, it is evident from reading the Examiner's description of the Srivastava reference that the Examiner is basing the rejection on US Pat. No. 6,475,490, filed Oct. 19, 1998, rather than US Pat. No. 6,007,821. As noted by the Examiner, US Pat. No. 6,475,490 teaches a method of treating tissue disrupted by atherosclerosis that is a typical vascular disorder state or treating ischemia that is a type of vascular disorder comprising administering HSP90. The entire disclosure of Srivastava, with one possible exception noted

below, is directed to HSPs other than HSP60/65. The singular possible exception arises from the passage beginning at column 4, line 59, and ending at column 5, line 8, quoted below:

To date, three major families of hsp have been identified based on molecular weight. The families have been called hsp60, hsp70, and hsp90... It is contemplated that hsps/stress proteins belonging to all of these three families can be used in the practice of the instant invention.

The entire remainder of the US Pat. No. 6,475,490 disclosure is directed wholly to HSP90 and HSP70. As stated by the Examiner at page 5 of the Office Communication, with reference to the enablement rejection, each class of HSP is both structurally and functionally divergent.

Applicants therefore submit that the disclosure of US Pat. No. 6,475,490 is insufficient with respect to HSP60/65 to provide a basis for asserting the obviousness rejection against claims 1, 3-7, 11, 19, and 31 as they are currently amended to be limited to methods involving HSP60/65 and therapeutically effective fragments and analogs thereof.

Second, the Wick reference provides a teaching away from making the combination proposed by the Examiner. The reference by Wick et al. teaches that (1) the earliest stage of atherogenesis consists of an autoimmune reaction against HSP60; and (2) because HSP60 quantitatively and qualitatively constitute very important antigenic components of bacteria and viruses, nearly all human beings show humoral and cellular immune reactivity against them. Wick et al., page S 445 bottom left column and middle right column. Further, Wick et al. go on to teach that all individuals have antibodies and T cells, respectively, recognizing HSP60 epitopes that confer cross-reactivity between microbial (bacterial, parasitic, viral) and human HSP60. Wick et al., page S448, second paragraph. Based on these teachings, one would avoid administering HSP60 to a human subject in order to treat atherosclerosis because according to Wick et al. administration of HSP60 (1) would induce an autoimmune reaction involved in the earliest stage of the very condition intended to be treated (i.e., atherogenesis), and/or (2) would be ineffective because nearly all human beings already possess humoral and cellular immune reactivity against HSP60.

In view of the foregoing, the cited references provide no sufficient suggestion or motivation to make the combination suggested by the Examiner, and, further, even if one were to make the suggested combination, there would be no reasonable expectation of successfully arriving at the claimed invention. Therefore, Applicants respectfully submit that the Examiner has failed to make a *prima facie* case for the rejection of claims 1, 3-7, 11, 19, and 31 under 35 U.S.C. § 103(a). Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1, 3-7, 11, 19, and 31 under 35 U.S.C. § 103(a).

Summary

Applicants believe the claims are in condition for allowance. An early and favorable response is earnestly solicited.

Respectfully submitted,
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